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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,896	01/24/2000	Matthew J. During	102194-6	9210

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/491,896	DURING, MATTHEW J.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,13-25,27,28,33-40,47-58,62-69,77-90,95-97,102-104 and 109* is/are pending in the application.

4a) Of the above claim(s) *4,13-21,33-35,47-53,55-58,62-67,69 and 77-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-8,22-25,27,28,36-40,54,68,86-90,95-97,102-104 and 109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-8,13-25,27,28,33-40,47-58,62-69,77-90,95-97,102-104 and 109* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Prosecution Application

The Request for Continued Examination (RCE) filed on 17 February 2004 under 37 CFR 1.114 based on parent Application No. 09/491,896 is acceptable and an RCE has been established. An action on the RCE follows.

Status of Application, Amendments and/or Claims

The amendment of 17 February 2004 has been entered in full. Claims 1, 6, 22, 24-25, 27, 36, 38, 54, 68, 86, 95, and 102 are amended.

This application contains claims 4, 13-21, 33-35, 47-53, 55-58, 62-67, and 77-85 drawn to an invention nonelected without traverse in the Response of 06 December 2000. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

It is noted that the amended independent claims now correspond to the originally elected invention of a method of treatment, improvement, or modification of a neurological disorder comprising administering an amino acid vaccine comprising a therapeutically effective amount of an antigen. Therefore, previously withdrawn claims 1-3, 5-8, 22-25, 27-28, 36-40, 54, 68, 86-90, 95-97, and 102-104 are rejoined with claim 109.

Claims 1-3, 5-8, 22-25, 27-28, 36-40, 54, 68, 86-90, 95-97, 102-104, and 109 are under consideration in the instant application.

Claim Rejections - 35 USC § 112

1. Claims 1-3, 5-8, 22-25, 27-28, 36-40, 54, 68, 86-90, 95-97, 102-104, and 109 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-3, 5-8, 22-25, 27-28, 36-40, 54, 68, 86-90, 95-97, 102-104, and 109 recite a method for modifying the function of a target receptor associated with a neurological disorder in a subject, a method for modifying the function of a target receptor associated with a neurological disorder in the central nervous system of a subject, a method for modifying the function of a target receptor associated with cognition in the central nervous system of a subject, a method for modifying the function of a target receptor associated with a neuroendocrine disorder in the central nervous system of a subject, a method for modifying the function of an N-methyl-D-aspartate (NMDA) target receptor associated with a neurological disorder in a subject, and a method for modifying the function of a N-methyl-D-aspartate (NMDA) target receptor associated with a neurological disorder or cognition in the central nervous system of a subject. Each recited method comprises administering either a vaccine comprising a therapeutically effective amount of an antigen wherein the antigen elicits the production of antibodies in the circulatory system of the subject, wherein the antibodies bind to a target receptor on a neuronal cell in the central nervous system and modify the function of the target receptor or a vaccine comprising a therapeutically effective amount of an antigen in the circulatory system wherein the antigen elicits the production of antibodies. The basis for this rejection is set forth for claim 109

at pg 5-12 of the previous Office Action (05 May 2003) and at pg 3-7 of the Office Action of 27 August 2001.

Applicant's arguments (17 February 2004) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that in light of submission of the declaration of Dr. Matthew During and the manuscript under 37 CFR § 1.132, claim 109 is fully enabled. Applicant contends that the declaration provides evidence to support the concept that peptide antigens elicit the production of antibodies, that the antibodies are present in the circulatory system, and that these antibodies are able to cross the blood-brain barrier and modify the function of the target receptor. Applicant also indicates that the modification of the target receptor can result in neuroprotection, improvement in cognitive function, as well as endocrine disorders that involve the same target receptor. Applicant also contends that the results described in the manuscript clearly demonstrate that the teachings provided in the specification are sufficient guidance for one skilled in the art to obtain similar results with the use of only routine experimentation. Applicant states that experiments were used to show that protein vaccination with peptide antigens of NMDA receptor leads to neuroprotection and to resistance against seizures.

Applicant's arguments have been fully considered but are not found to be persuasive. The declaration of Dr. Matthew During and the manuscript filed 17 February 2004 under 37 CFR § 1.132 is insufficient to overcome the rejection of claims 1-3, 5-8, 22-25, 27-28, 36-40, 54, 68, 86-90, 95-97, 102-104, and 109 under 35 U.S.C. § 112, first paragraph as set forth in the last Office Action. Although the experiments in the unpublished manuscript indicate that *specific* NMDAR1 antigens stimulate an immune response having anti-epileptic affects (seizure latency

and progression) and protect against hippocampal cell death, the declaration is not persuasive. Specifically, the NR1 antigens (NR1[21-375], NR1[654-800]), the rat models of epilepsy, and other methods discussed by Dr. During and by the manuscript are not disclosed in the specification of the instant application as originally filed. The specification provides no guidance or working examples for the administration of a NMDAR1 antigen peptide vaccine and modification of the function of any target receptor in a subject, particularly by utilizing NR1[21-375], NR1[654-800] and rat models of epilepsy. The examples in the specification only disclose the delivery of the full length mouse NMDAR1 *gene* into rats. The working examples in the specification directed to administration of the genetic vaccine do not provide guidance regarding the administration of a protein vaccine to subjects.

Additionally, the evidence disclosed in the declaration and manuscript is not commensurate in scope with the claims of the instant application. For example, the instant claims do not recite any *specific* antigen to be administered or the identity of the target receptor. This is unlike the During declaration and manuscript which indicate that NR1[21-375] and NR1[654-800] antigens are administered to generate antibodies that target specific domains in NMDA receptor subunits. The claims also do not recite that the peptide antigens have anti-epileptic effects or reduce neuronal loss in regions of the hippocampus. Therefore, undue experimentation would still be required of the skilled artisan to administer any antigen or any NMDA antigen in the circulatory system of the subject, wherein the antigen elicits the production of antibodies that pass into the CNS and bind any target receptor located on any neuronal cell. A large amount of experimentation would also be required of one skilled in the art to modify the function of a target receptor associated with a neurological disorder in a subject, to

modify the function of a target receptor associated with a neurological disorder in the central nervous system of a subject, modify the function of a target receptor associated with cognition in the central nervous system of a subject, to modify the function of a target receptor associated with a neuroendocrine disorder in the central nervous system of a subject, to modifying the function of an N-methyl-D-aspartate (NMDA) target receptor associated with a neurological disorder in a subject, and to modify the function of a N-methyl-D-aspartate (NMDA) target receptor associated with a neurological disorder or cognition in the central nervous system of a subject. Additionally, there is no guidance or working examples in the specification itself to indicate that if administered, an antigen (particularly an NMDA antigen) produces antibodies and that the antibodies bind to a target receptor on a neuronal cell to directly modify the receptor or indirectly modify the function of a process involving the receptor *in vivo*.

(ii) Applicant asserts that claim 109 is limited to antibodies that bind to a target receptor located on a neuronal cell in the CNS of the subject and associated with a [neurological] disorder. Applicant submits that the claim does not cover any or all neuronal cells. Applicant contends that the claim is only directed to neuronal cells that have the desired target receptor and that are associated with neurological disorders, a neuroendocrine disorder, or cognition. Applicant argues that not all neuronal cells will express the NMDA receptor, for example. Applicant states that a subset of neuronal cells does express the NMDA receptor and it is on these cells that the NMDA receptor is modified by binding of the NMDA antibody. Additionally, Applicant asserts that the claims have been amended so that they no longer recite a variety of target receptors, but simply a neuroreceptor, i.e., a receptor present on a neuronal cell.

Applicant's arguments have been fully considered but are not found to be persuasive. There is little or no guidance provided in the specification that indicates which specific neuronal cells have a desired target receptor and are also associated with neurological disorders, a neuroendocrine disorder, or cognition. There are a variety of neuronal cells of the CNS that may or may not be encompassed by the claimed methods, such as dopaminergic neurons, serotonergic neurons, motor neurons, sensory neurons, mesencephalic neurons, hippocampal hilar neurons, oligodendrocytes, Schwann cells, and astrocytes, among others. Undue experimentation would be required of the skilled artisan to determine which specific neuronal cells express the appropriate target receptor and are also associated with a neurological disorder. Undue experimentation would also be required of the skilled artisan to even determine which region of the CNS should be targeted with the antigen/antibodies. Different types of neuronal cells express different populations of receptors and one skilled in the art cannot assume that all neuronal cells in the central nervous system will express any and all target receptors recited in the claims.

Independent claims 1, 22, 36, and 54 do not recite the administration of a specific antigen or a specific receptor or neuronal cell that is to be targeted. Additionally, although independent claims 86, 95, 102, and 109 recite an NMDA target antigen and an NMDA target receptor, undue experimentation would be required of the skilled artisan to determine which specific NMDA target antigen is administered and what specific neuronal cells the NMDA target receptor is located on. The specification of the instant application only outlines a prophetic procedure for administering an antigen vaccine into the circulatory system of a subject. The present invention is unpredictable and complex wherein one skilled in the art may not necessarily

modify the function of a target receptor associated with a neurological disease. Although the claimed method may utilize routine administration techniques, the results of the method are unpredictable and complex when combined with the step of administering any antigen, particularly any NMDAR1 antigen. It is noted that according to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed".

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to modify the function of a target receptor associated with a neurological disorder, cognition, or neuroendocrine disorder by administration of an antigen vaccine and to determine an activity of other NMDA receptor subunit family members, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the response and longevity of the antigen vaccine *in vivo*, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, and the breadth of the claims which embrace all possible neuronal cells and all possible target receptors, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C Kemmerer

BEB
Art Unit 1647
05 May 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER